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A Clinical Trial of Oxfendazole-PLO formula for treatment of T. foetus in bulls Phase II

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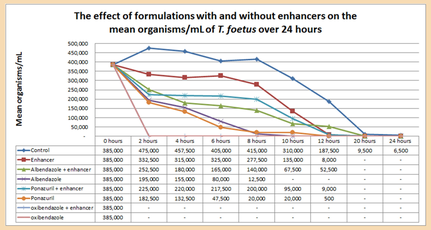
Abstract

- 13 yrs of in vitro studies & in vivo trials led to the a patented topical Oxfendazole +plus/PLO gel formulation.
- Oxfen+ PLO gel has efficacy in vitro & in vivo for killing *Tritrichomonoasis foetus (T. foetus)*
- Clinical trials, phase 2 - more bulls using a higher dose of the Oxfendazole



	0 hours	2 hours	4 hours	6 hours	8 hours	10 hours	12 hours	20 hours	24 hours
Control	385,000	475,000	457,500	405,000	415,000	310,000	187,500	9,500	6,500
Enhancer	385,000	332,500	315,000	325,000	277,500	135,000	8,000	-	-
Albendazole + enhancer	385,000	252,500	180,000	165,000	140,000	67,500	52,500	-	-
Albendazole	385,000	195,000	155,000	80,000	12,500	-	-	-	-
Ponacuril + enhancer	385,000	225,000	220,000	217,500	200,000	95,000	9,000	-	-
Ponacuril	385,000	182,500	132,500	47,500	20,000	20,000	500	-	-
oxibendazole + enhancer	385,000	-	-	-	-	-	-	-	-
oxibendazole	385,000	-	-	-	-	-	-	-	-

Figure 1. in vitro trials of T. foetus cultured with benzimidazoles & PLO gels

Introduction

- Bovine trichomoniasis (Trich) is a venereal disease of cattle caused by the protozoan *T. foetus*.
- *T. foetus infections* cause infertility, abortions, metritis, with resultant low calf crops.
- The bull is the asymptomatic carrier & spreads infection to cows & heifers during breeding.
- This study examined efficacy following topical treatment with Oxfendazole +PLO gel on the penis & prepuce of naturally infected *T. foetus* bulls along with oral administration of Oxfendazole.
- Oxfendazole is not absorbed very well orally in cattle but use of PLO gels allows for topical & systemic absorption. Culture, & RTPCR were used to document if live organisms & *T. foetus* DNA were present following treatment. A dose response study is underway to develop the most efficacious & safe treatment.
- Testing for evidence of drug in plasma, liver, urine & tissue levels to meet goals toward FDA compliance of drug approval in food animals will be completed to meet residue requirements to assure that any animal that is going to be used for human consumption is drug free or within the tolerable level (1.7 ppm in the liver).

Methods

- A total of six Bulls naturally infected with *T. foetus* were enrolled in the study. All bulls underwent serial collection of smegma via preputial scrapings with a Pizzel stick (Lane Manufacturing) followed by testing of smegma for *live organisms & T. foetus DNA* via culture & RTPCR, respectively. Samples were collected in duplicate. The smegma was placed in a vial of Modified Diamond's Media and submitted to the Thompson, Bishop, Sparks, Alabama, Diagnostic Laboratory. All cultures were examined for a period of seven days and examined for live organisms initially and every 48 hrs. Prior to the RTPCR the smegma sample was cultured for live organisms for 48 hours to allow for amplification *of T. foetus* in the sample.
- Temperature studies and pH of the prepuce were recorded to determine the best polymers to use for drug release. The PLO+ Oxfendazole patented formulation was prepared in a pharmacology laboratory using aseptic technique & USP compounding guidelines. The drug and vehicle were homogenized electronically at 1000 RPMs for 15 minutes. The second phase study increased the dosage of Oxfendazole by 25%. which showed less T. foetus DNA detected & negative cultures for live organism.
- All formulations were topically applied to the penis and the prepuce by a licensed veterinarian. The bulls were tabled and sedated with acepromazine for treatment application. The bulls were tested bi-weekly to weekly for efficacy. Additional applications of the product were administered until efficacy was established.
- Oral Fendbenazole (Synthantic®) was also administered at each treatment to aid systemic elimination of *T. foetus* from potential reservoir sites such as the urethra. A concurrent study showed the urethra is a reservoir site for *T. foetus* in naturally infected *T. foetus* bulls.

Results

Clinical Trials – PLO & Oxfendazole

- 6 bulls utilized in the study.
- 4 bulls culture negative for 6 weeks
- 1 bull negative for 11 months
- CT values – reduction in *T. foetus* DNA
- 3 euthanized following Tx had PCR & culture negative of reproductive tract including urethra

64BJW5921 Culture 0.0 NEGATIVE 1
64BJW5922 Culture 32.5 POSITIVE 1

https://www.medisca.com/NDC_SPECS/MUS/2340/image/2340-08_MUS.jpg

Conclusions

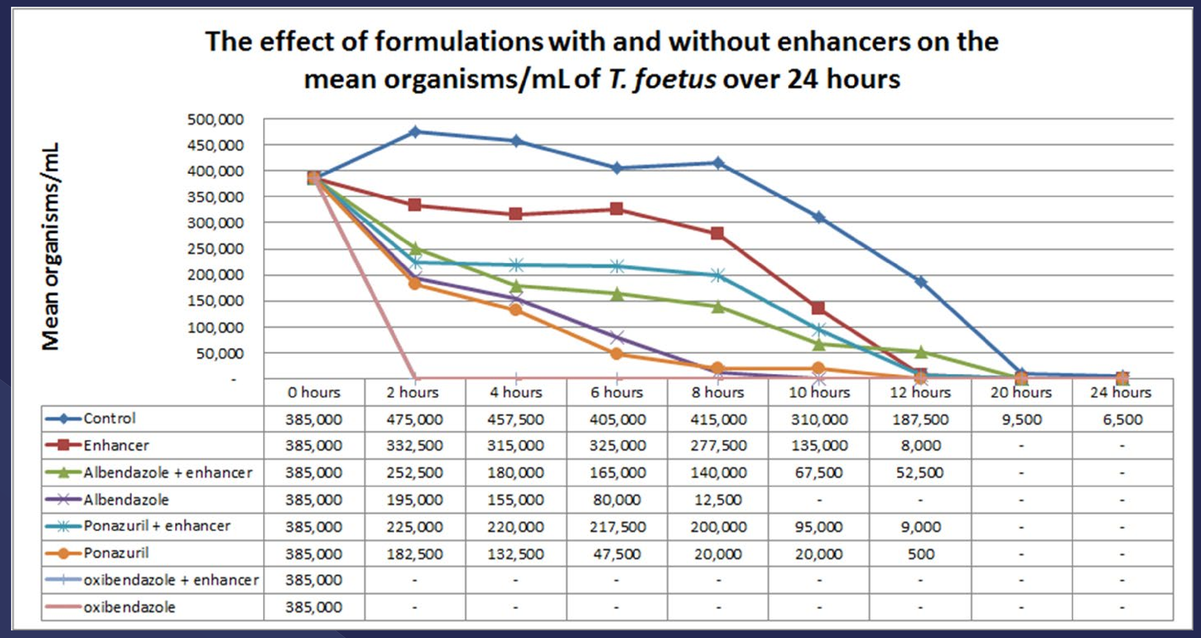
In-vitro studies & in-vivo studies, including phase 2, have shown efficacy with the patented OxF+PLO gel. A larger clinical trial is in the process of being conducted to prove the most efficacious dosage needed to treat *T. foetus*. Currently, bulls that are positive cannot be breed and have to be euthanized. Boehringer-Ingelheim pharmaceutical company has a vaccine that is 60% effective for heifers. However an approved bull therapy is not available for bulls. The next study will administer the drug daily for 5 days rather than a single dose to achieve a negative RTPCR in addition to negative cultures.

Funding is from the Auburn University Launch Innovation Program & the Merck Merial Student Program:

- Sue Duran & Julie Schnuelle Co-PI

Solution- Development of a topical treatment

- After 13 years of in-vitro testing of formulations that kill T. foetus.
- patent on a group of benzidamizoles and ponazuril.
- Oxfendazole, an anti-protozoal and dewormer that has been mixed with a long acting vehicle (PLO) gel that kills the infection.
- One bull has been tested with a kill for 14 days.



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Funding for more clinical studies are need ed to be completed on a larger number of animals to determine the most effective dosage and frequency of treatments.